Review

MEDICINE PALLIATIVE CARE

DOI: 10.47582/jompac.1617224

J Med Palliat Care. 2025;6(2):159-166

Substance use and memory impairments: a multidimensional review on neurological and cognitive effects

Gün Pakyürek

Department of Psychology, Faculty of Science and Letters, İzmir Democracy University, İzmir, Turkiye

Cite this article as: Pakyürek G. Substance use and memory impairments: a multidimensional review on neurological and cognitive effects. *J Med Palliat Care*. 2025;6(2):159-166.

Received: 10.01.2025 • **Accepted**: 17.03.2025 • **Published**: 23.03.2025

ABSTRACT

This study aimed to examine the relationship between substance use and memory disorders. This study also analyzed the biological effects of drug use on the brain and investigated the mechanisms by which these effects lead to impairment of memory function. Furthermore, the impact of various elements, including substance abuse, mental health conditions, hereditary susceptibility, and chronological age, was assessed. Substance use negatively affects memory and learning processes by causing functional impairments in critical regions such as the hippocampus and frontal lobe. Different substances cause specific damage to the memory. This review highlights how substance use can lead to permanent neurocognitive impairment, with effects varying according to substance type, duration of use, and individual factors. This underscores the importance of early intervention and preventive strategies. Multidisciplinary approaches are important in the prevention and management of these effects.

Keywords: Substance addiction, memory disorders, cognitive effects

INTRODUCTION

Substance use and addiction are considered important public health problems that create complex effects not only at the individual level but also on a social and global scale. Recent studies have emphasized the escalating global burden of substance use disorders, necessitating updated reviews. To understand this phenomenon and to develop effective intervention methods, there is a need to comprehensively address the prevalence, causes, and consequences of substance abuse. This study aims to fill a gap in the literature by synthesizing evidence on how substance use impairs memory, a critical yet underexplored cognitive outcome, compared to broader addiction research. Researchers have developed various theoretical approaches to explain the effects of substance use on individuals and the mechanisms underlying these effects and have presented experimental findings that support these approaches.

According to the 2023 World Drug Report published by the United Nations Office on Drugs and Crime, approximately 296 million people aged 15-64 used drugs at least once in 2022, an increase from 275 million in 2021, reflecting a growing challenge.[1] This rate is significantly higher among men than women. In Turkey, 6.1% of men and only 0.3% of women use drugs at some point in their lives.[2] When the relationship between substance use and socioeconomic conditions is analyzed, factors such as low-income level, unemployment, and low education level increase the prevalence of this problem. Social factors such as gender roles and cultural norms also shape substance use tendencies. The causes and dynamics of substance use can be explained using various theoretical frameworks. These frameworks consider substance use a complex interaction of biological, psychological, and social factors, encompassing a wide range of influences that lead individuals to such behaviors.

The biopsychosocial model is a multifaceted approach that explains substance use through the interaction of biological, psychological, and social factors. Genetic predisposition, neurobiological processes, personality traits, family structure, environmental stress factors, and cultural norms were the main components of this model. Research has emphasized the role of genetic factors in the development of addiction. Kreek et al.[3] suggested that genetic components of addiction predisposition can explain approximately 30% of addictive behaviors, which was updated by Wright et al.[4] The genetic basis of substance use remains a key focus of addiction research. The effects on the dopamine system are among the neurobiological mechanisms underlying addiction. The allostasis theory, developed by Koob and Le Moal,[5] argues that addiction leads to continuous adaptation in the brain's reward system, making it a chronic condition.[5,6] This theory explains the long-term negative effects of substance addiction on brain neuroplasticity. Psychological coping skills related to stress and emotional regulation strategies are also critical factors that affect susceptibility to addiction.

The examination of substance use within the framework of the social learning theory reveals the importance of

Corresponding Author: Gün Pakyürek, gunpakyurek@gmail.com

This work is licensed under a Creative Commons Attribution 4.0 International License.

environmental influences and observational learning. Bandura's[7] theory posits that individuals can learn substance use by observing and modeling behaviors around them. Peer influence and role models encourage substance use, especially among the youth. Positive reinforcement mechanisms motivate their continued use. Agnew's[8] tension theory suggests that efforts to cope with stress and social pressure may trigger substance use. Socioeconomic problems, family conflicts, and unemployment often drive individuals toward alcohol or drugs.[9] Studies show that those experiencing economic difficulties are more likely to turn to substances. Subculture theory argues that certain social groups normalize substance use, reinforcing a sense of belonging, particularly in youth subcultures. Cohen's[9] subculture theory suggests these groups strengthen individuals' willingness to challenge social norms. Psychodynamic theory links substances to early life experiences and unresolved internal conflicts. Khantzian[10] defined addiction as an attempt to alleviate psychological pain, noting higher risks in individuals with childhood trauma. These theoretical approaches to substance use explain different aspects of the phenomenon and contribute to a multidimensional understanding. However, each of these theories focuses on only one specific aspect of substance use, and does not fully reflect the complexity of the situation. These frameworks collectively suggest a multifaceted etiology, necessitating holistic interventions.

Substance abuse and addiction are complex problems that reduce the quality of life of individuals, consume social resources, and threaten public health globally. Among the negative effects of this problem, memory impairment, which also affects cognitive skills, is particularly important. These impairments in memory processes indicate that substance use can negatively affect individuals' daily lives and functionality. In this context, the causes of theoretical approaches to memory disorders help us better understand this complex problem.

MEMORY DISORDERS

Memory disorders are among the most complex and multidimensional cognitive problems. Theories explaining these disorders have shed light on various aspects of memory processes, offering perspectives from cognitive psychology, neuroscience, and neuropsychology. The neuroplasticity theory of memory disorders focuses on the brain's capacity to change and adapt.[11] This theory suggests that memory disorders arise from the weakening or loss of synaptic connections, a mechanism critical in neurodegenerative diseases such as Alzheimer's and substance abuse.[11] In Alzheimer's patients, the loss of neurons in the hippocampus and other limbic system structures and the decrease in synaptic connections cause individuals to experience serious difficulties in the process of forming and storing new memories.[12] Studies show that beta-amyloid plaque accumulation disrupts synaptic plasticity, directly affecting short-term memory. This theory also applies to memory deficits caused by traumatic brain injury, epilepsy, and substance abuse. The processing speed theory explains memory impairments related to aging and substance use.[13] A decrease in information-processing speed with age negatively affects working memory performance, causing difficulties in encoding and recalling new information. Research indicates that older individuals process information more slowly than younger ones, impacting memory, especially during multitasking.[13] For example, an elderly individual's difficulty in remembering a recently learned phone number is due to their inability to process information quickly enough, and chronic alcohol users show a 20% reduction in processing speed, leading to significant declines in short-term and working.[14] The decrease in white matter density with age or substance-induced damage slows neural transmission further. According to this theory, substance use, especially long-term consumption of substances that damage the central nervous system, leads to a significant decrease in the speed of cognitive processes and this slowdown in processing speed directly affects memory processes and creates difficulties in encoding, storing and recalling new information.[15,16] Substances like alcohol, cocaine, and cannabinoids damage nerve cells or disrupt neurotransmitter balances, exacerbating this slowdown.[17] Longitudinal studies of methamphetamine users confirm reduced processing speed impacts episodic memory.[17] These findings emphasize that the processing speed theory provides a powerful model to explain substance use-induced memory impairments and the importance of focusing on processing speed in cognitive rehabilitation processes of substance use.

The Activation-Monitoring Theory explains memory errors and false memories. This posits that recalling information activates related data, sometimes leading to false recall. This is common in eyewitness cases, where details heard later are misremembered as true. For example, a crime witness's recollection of details that he/she did not see at the time of the incident but heard later as a true memory can be explained by this theory.[18] Laboratory studies show that false information can integrate into memory processes, facilitating false memories.[19] Substance use increases source errors by disrupting neurotransmitter activity in the prefrontal cortex and hippocampus.[20] For example, experiments in individuals under the influence of alcohol have shown that false memories frequently increase because of weakened memory monitoring mechanisms.[21] Similarly, a study in individuals using cannabis found that they were more likely to falsely link memory sources under the influence of the substance.[22] These findings suggest that activation-monitoring theory states that specific memory errors, such as false memories, may occur more commonly as a result of substance use. Alcohol weakens memory monitoring mechanisms, increasing false memories, while cannabis use heightens the likelihood of misattributing memory sources.[23]

The Fuzzy Trace Theory posits two memory systems: verbatim traces for detailed recall and gist traces for general meaning. Memory impairments often involve loss of verbatim traces, making detailed recall difficult. This theory explains why some individuals have difficulty remembering specific details while remembering general information.[24] For example, in neurological examinations, it has been observed that patients with dementia can recall the general outline of an event but cannot provide clear information about its details. The loss of specific traces makes it difficult to maintain the clarity and detail of memories. Patients with dementia, for instance,

recall events that are outline, but not specific. Substance abuse, particularly alcohol and drugs, weakens verbatim traces, leading to reliance on gist traces and inaccurate recall.[25] Multiple Trace Theory suggests episodic memories are reconstructed over time through multiple neural traces between the hippocampus and cortical areas. Substance abuse disrupts these traces, weakening episodic memory and making it less detailed over time.[26]

Theories explaining memory disorders provide an in-depth understanding of the factors that influence cognitive functioning, showing how both neurological and environmental influences are reflected in memory processes.[27,28] Each theory emphasizes different aspects of memory mechanisms, and details the effects of substance use on impairments in these mechanisms. In this context, substance use appears to have multifaceted effects, ranging from synaptic plasticity to the reconstruction of episodic memories, from decreased processing speed to the formation of false memories.[29] The explanations offered by these theories provide an important basis for understanding the multidimensional effects of substance use on memory.[30] In which the complex effects of substance use on memory will be elaborated, and reflections of this situation on cognitive functions will be discussed.

METHODS

This review systematically analyzes the current scientific literature on the relationship between substance use and memory impairments. Studies were selected based on predefined inclusion and exclusion criteria, and relevant data sources were systematically searched using specific keywords. The data for this study were obtained from major scientific databases including PubMed, PsycINFO, Scopus, and Web of Science. Peer-reviewed articles published between 2010 and 2024 were prioritized, with a focus on both empirical research and meta-analysis. Case reports, letters to the editor, and print articles were excluded. Studies were selected based on specific inclusion criteria such as examining the relationship between substance use and memory processes, assessing memory functions through neuropsychological measures, and including human participants in experimental or observational designs. Exclusion criteria included studies that relied solely on animal models, had small sample sizes or significant methodological limitations, and did not specifically assess memory-related outcomes in substance users.

A comprehensive literature search was conducted using Boolean operators (AND, OR) to combine relevant keywords, including "substance use" AND "memory impairment," "drug abuse" AND "cognitive decline," "alcohol use" AND "working memory," "neurotoxicity" AND "memory function," and "cannabis" AND "episodic memory." The search results were filtered, and only studies that met the eligibility criteria were included in the analysis.

The selected studies were analyzed using a content analysis approach to compare the findings across different research methodologies. The findings were categorized into key themes such as the neurobiological mechanisms underlying substance-induced memory impairments, variations in memory deficits based on substance type, and the impact of age on cognitive decline related to substance use. This methodological framework ensures a systematic and comprehensive approach for understanding the multifaceted effects of substance use on memory processes. This analysis provides insights into how different substances affect memory functions and highlights the importance of early intervention strategies.

MULTIDIMENSIONAL EFFECTS OF SUBSTANCE USE ON MEMORY

The relationship between substance use and memory disorders is complex and multifaceted. This relationship stems from various factors, such as the direct effects of substance use on the brain, chronic use leading to neurological changes, and the effects of substance use disorder on the lifestyle of individuals.[31] The mechanisms underlying this relationship have been discussed in detail in the literature, and a better understanding of these mechanisms is important for developing strategies to solve this problem. Recent studies have revealed important findings on this issue by examining the different dimensions of substance use more comprehensively.

Substance use exerts multifaceted effects on memory through direct neurotoxic effects and indirect lifestyle changes. Chronic alcohol consumption, for example, has been associated with a reduction of hippocampal volume by up to 15%, leading to significant episodic memory deficits and even neurological conditions such as Wernicke-Korsakoff syndrome.[32,33] Cannabinoids have also been reported to weaken learning processes by affecting glutamate release in the brain.[34] The effects of substance use on neurotransmitter systems further complicate memory processing and storage processes.[35] Volkow and Fowler[30] revealed that imbalances in dopamine systems directly negatively affect cognitive performance, especially by affecting motivation and reward perception. Chronic substance use causes long-term changes in structural and functional properties of the brain. Long-term methamphetamine use has been shown to cause neuronal death and decrease synaptic connections in regions such as the frontal lobe, caudate nucleus, and hippocampus.[36] Such damage may permanently affect cognitive functions, such as self-control, decision-making, and memory. Pfefferbaum and Sullivan[37] demonstrated that chronic alcohol use causes severe disruptions in white matter structure and a marked decrease in neurocognitive performance. Similarly, neurological diseases such as Wernicke-Korsakoff syndrome occur due to alcohol use and increase the severity of memory impairments. In addition, cocaine use has been reported to cause irreversible damage to the dopaminergic system of the brain, leading to long-term problems in memory processes.[38]

The effects of substance use disorder on lifestyle indirectly negatively affected memory function. For example, substance use leads to disruptions in sleep patterns and malnutrition.[39] Lack of sleep negatively affects synaptic reorganization, which is a critical process in memory consolidation, making it difficult to learn and store new information.[40] In addition, studies on malnutrition have shown that vitamin B deficiency negatively affects neuronal health and memory function.[41] For example, Falletti et al.[42] reported that vitamin deficiencies that

occur during substance abuse lead to more serious memory problems, especially in individuals who consume alcohol.

The effects of substance use depend on the type of substance being used. While alcohol has more pronounced negative effects on episodic memory, amphetamine and cocaine, which are stimulant substances, affect working memory and attention processes.[43] Substances with strong neurotoxic effects, such as methamphetamine, cause more rapid and permanent brain damage than other substances.[44] In addition, the depressant effects of opioids affect an individual's memory performance in a more complex manner by impairing decision-making and emotional processing. Ersche et al.[45] reported that long-term cocaine use leads to a significant decrease in working memory capacity. In this study, the effects of long-term cocaine use on cognitive function were addressed, especially changes in working memory capacity. This study was based on comparisons between long-term cocaine users and healthy controls. Participants were administered various neuropsychological tests, and their working memory capacity, attentional control, and executive function were assessed. The results revealed that cocaine users experienced a marked reduction in working memory capacity compared with the control group. This reduction was associated with difficulties in holding and manipulating information over short periods. The researchers explained this by the fact that cocaine disrupts the neurotransmitter balance in the prefrontal cortex and negatively affects neural plasticity. Furthermore, these cognitive impairments were observed to increase with duration and intensity of use.

AGE EFFECT ON SUBSTANCE USE AND MEMORY DISORDERS

The age at which substance use begins plays a crucial role in determining the severity and longevity of memory and cognitive impairments. The adolescent brain, which is still in a critical phase of development, is particularly vulnerable to the neurotoxic effects of substance use. During this period, the brain undergoes significant structural and functional changes, with key processes such as synaptic pruning, myelination, and strengthening of neural circuits. These developmental changes make the brain more susceptible to the damaging effects of drugs and alcohol, potentially leading to long-term deficits in cognitive function, including memory, attention, and executive function.

Research has consistently shown that early substance use during adolescence can cause irreversible damage to the brain regions responsible for memory processing, such as the hippocampus and prefrontal cortex. For instance, studies have demonstrated that adolescent alcohol use leads to a reduction in hippocampal volume, which is linked to difficulties in episodic memory and learning.[32] Furthermore, substance use during adolescence disrupts the development of the prefrontal cortex, a brain region involved in working memory, decision making, and impulse control, thereby impairing cognitive abilities that are critical for academic and social functioning.

One of the key factors contributing to adolescents' vulnerability to substance-induced memory deficits is the high degree of neuroplasticity during this stage of life. While neuroplasticity allows for learning and adaptation, it also means that the brain is easily altered by external factors, including substance use. The neurotoxic effects of substances such as alcohol, marijuana, and stimulants can interfere with the normal brain maturation process, potentially leading to enduring cognitive deficits. For example, chronic cannabis use during adolescence has been associated with long-term impairments in working memory and executive function.[19]

The long-term impact of adolescent substance use on memory is compounded by the fact that many individuals who begin using substances at an early age are at a higher risk of developing substance use disorders later in life. The combination of early exposure to substances and development of substance use disorders significantly increases the likelihood of developing cognitive deficits in adulthood. Studies have shown that individuals who began using alcohol or other drugs in their teenage years exhibit more pronounced cognitive decline in adulthood compared to those who initiated use later in life.[46,47]

In addition to the direct neurotoxic effects of substances on the developing brain, lifestyle changes associated with early substance use, such as poor nutrition, disrupted sleep patterns, and increased risk of mental health issues further exacerbate memory problems. The impact of poor nutrition, for example, is particularly concerning during adolescence, which is marked by rapid physical and cognitive growth. Deficiencies in essential nutrients, such as vitamin B and omega-3 fatty acids, can impair neuronal function and exacerbate memory deficits in adolescents who use substances regularly.[42]

Recent studies have also highlighted the role of genetic factors in shaping adolescents' vulnerability to substance-induced memory impairments. Genetic variations in genes involved in neurotransmitter systems, such as COMT and BDNF, may predispose some individuals to severe cognitive deficits following substance use. Adolescents with these genetic predispositions may experience a greater degree of neurotoxic damage to brain structures involved in memory, making them more susceptible to long-term cognitive impairments.[4]

Moreover, the effects of early substance use were not limited to memory deficits. Adolescents who engage in substance use are also at risk of developing other cognitive and emotional challenges, including difficulties with attention, problem-solving, and emotional regulation. When combined with the social and academic pressures that adolescents face, these cognitive impairments can have a lasting impact on their overall well-being and development. As these individuals transition into adulthood, the consequences of early substance use can persist, potentially affecting their ability to succeed in the workforce and to maintain healthy relationships.

GENETIC FACTORS ON SUBSTANCE USE AND MEMORY DISORDERS

Genetic factors play a crucial role in mediating the relationship between substance abuse and memory disorders. While environmental influences, such as early exposure to substances and lifestyle factors, undoubtedly contribute to cognitive impairment, genetic predisposition can significantly amplify or modulate the effects of substance use on brain

function, particularly memory. Research into the genetic underpinnings of substance use disorders (SUDs) and their neurocognitive consequences has revealed important insights into why certain individuals are more susceptible to substance-induced memory deficits than others. One of the key areas of focus in genetic studies of substance use and memory is the role of neurotransmitter systems, particularly those involving dopamine, glutamate, and serotonin. Variations in the genes that regulate these systems can influence how the brain responds to substances and, subsequently, how memory processes are affected. For instance, the gene encoding the catechol-COMT enzyme, which regulates dopamine metabolism in the prefrontal cortex, has been linked to individual differences in cognitive function. Studies have shown that individuals with certain COMT polymorphisms, specifically the Val158Met variant, may experience more severe cognitive impairments, including memory dysfunction, when exposed to substances such as alcohol or amphetamines.[4] This genetic variation may make the brain more vulnerable to neurotoxic damage, thereby increasing the risk of developing long-term memory deficits following substance abuse. Another gene of significant interest is brain-derived neurotrophic factor (BDNF), which plays a critical role in synaptic plasticity, learning, and memory. BDNF facilitates the growth, maintenance, and survival of neurons, and its expression is strongly influenced by environmental factors, including substance use. Genetic variants of the BDNF gene, particularly the Val66Met polymorphism, have been shown to impair hippocampal-dependent memory functions such as spatial memory and long-term memory consolidation. These genetic differences can make individuals with certain BDNF variants more susceptible to cognitive impairments associated with chronic substance use.[48] Furthermore, BDNF's role of BDNF in neuroplasticity means that individuals with impaired BDNF function may have a reduced ability to recover from the neurotoxic effects of substances, leading to persistent memory deficits even after abstinence. In addition to the genes involved in neurotransmitter regulation, recent research has also identified the role of genes related to neuroinflammation in substance-induced memory dysfunction. Substances such as alcohol, methamphetamine, and cocaine increase neuroinflammation in the brain, which can contribute to neuronal damage, particularly in regions such as the hippocampus that are essential for memory formation and consolidation. Variations in the genes that control the brain's immune response, such as those in the interleukin (IL) and tumor necrosis factor (TNF) families, can influence the degree of neuroinflammation that occurs in response to substance use. Individuals with certain genetic predispositions to higher levels of neuroinflammation may experience more severe damage to brain structures involved in memory, leading to more pronounced cognitive deficits.[11] The genetic susceptibility to memory disorders associated with substance use is not only a matter of individual genetic differences but also the interaction between genetic factors and the timing of substance use. For instance, individuals with a genetic predisposition to addiction and cognitive impairment may be especially vulnerable to the neurotoxic effects of substances when exposure occurs during critical periods of brain development, such as adolescence. During this stage, the brain still undergoes significant maturation, and the impact of substances such as alcohol or marijuana may be particularly damaging. In such cases, genetic vulnerabilities can be exacerbated by the early initiation of substance use, leading to long-term and often irreversible cognitive deficits, including memory impairments.[47]

The role of epigenetics in substance-induced memory dysfunction is gaining increasing attention. Epigenetic modifications, which involve changes in gene expression without altering the underlying DNA sequence, can be influenced by environmental factors such as substance use. These modifications can have lasting effects on brain functions, including memory. For example, research has shown that chronic substance use can lead to changes in DNA methylation patterns in brain regions involved in memory processes, such as the hippocampus. These epigenetic changes may not only affect the individual who is using substances but could also be passed down to future generations, potentially increasing the risk of memory impairments in offspring.[49]

The interaction between genetic factors and psychiatric conditions further complicates the relationship between substance use and memory disorders.[50,51] Psychiatric disorders, such as depression, anxiety, and schizophrenia, are often comorbid with substance use disorders, and genetic predispositions to these conditions may enhance vulnerability to cognitive impairments. For example, genetic risk factors for depression, such as polymorphisms in the serotonin transporter (5-HTT) gene, have been linked to increased susceptibility to cognitive deficits caused by substance use, particularly memory and attention.[52] Individuals with both genetic vulnerabilities to psychiatric disorders and a history of substance use may face compounded risks of memory dysfunction, highlighting the need for integrated treatment approaches.

THE RELATIONSHIP BETWEEN PSYCHIATRIC DISORDERS, SUBSTANCE USE, AND MEMORY

The intricate relationship between psychiatric disorders, substance use, and memory dysfunction underscores the complex interplay between genetic, neurobiological, and environmental factors that significantly impact cognitive functioning. Psychiatric disorders, such as depression, anxiety, posttraumatic stress disorder (PTSD), and schizophrenia, commonly co-occur with substance use disorders (SUDs), which complicate the cognitive and emotional processes associated with substance use, particularly memory. Research has demonstrated that substance use not only exacerbates psychiatric symptoms, but also negatively affects cognitive domains, including memory, attention, and executive functioning.

Memory deficits are frequently observed in individuals with psychiatric disorders even in the absence of substance use. For example, depression has been consistently linked to cognitive impairment, particularly in the areas of working and episodic memory. These deficits are thought to arise from neurobiological changes in brain regions, such as the

prefrontal cortex and hippocampus, which are essential for memory processing. A meta-analysis by McDermott et al.[53] revealed that individuals with major depressive disorder (MDD) exhibit significant impairments in verbal and non-verbal memory tasks. These impairments are believed to be mediated by the disruption of hippocampal neurogenesis and alterations in the serotonin and dopamine systems, which play critical roles in memory formation and consolidation. Furthermore, depressive symptoms, including low motivation and anhedonia, may indirectly impair memory by reducing engagement in cognitive activities and social interactions that are essential for cognitive preservation. Anxiety disorders also contribute to memory dysfunction, particularly by impairing the working memory and attentional control. Chronic stress, a hallmark of anxiety disorders, can increase levels of cortisol, a hormone that negatively affects hippocampal function. Elevated cortisol levels can disrupt the encoding and retrieval of memories, particularly in tasks that require attention and integration of new information. For instance, Zhang et al.[54] showed that individuals with generalized anxiety disorder (GAD) had lower scores on working memory tasks than healthy controls, with the degree of impairment being directly related to the severity of anxiety symptoms. This suggests that the persistent physiological and psychological stress associated with anxiety disorders may hinder the brain's ability to process and store new information.

Substance use, whether alcohol, illicit drugs, or prescription medications, has well-documented neurotoxic effects on memory, particularly episodic memory, working memory, and attention. As previously discussed, substances such as alcohol, methamphetamine, cocaine, and opioids can directly impair brain structures involved in memory processing, such as the hippocampus, prefrontal cortex, and the dopaminergic and glutamatergic systems. For example, chronic alcohol use is a major contributor to memory deficits, particularly alcohol-induced cognitive impairment (AICI) and Wernicke-Korsakoff syndrome (WKS). Alcohol-related brain damage leads to a significant reduction in hippocampal volume and disrupts synaptic plasticity, impairing both short-term and long-term memory processes.[32] The neurotoxic effects of alcohol are compounded by nutritional deficiencies, such as thiamine deficiency, which is common in individuals with alcohol use disorder (AUD) and further exacerbates memory dysfunction. Studies have shown that individuals with WKS, a severe form of alcohol-related cognitive impairment, experience profound deficits in episodic memory such as an inability to form new memories or recall recent events. Similarly, stimulant substances, such as methamphetamine and cocaine, can cause severe damage to the dopaminergic and glutamatergic systems, resulting in working memory deficits and impairments in executive function. For example, long-term methamphetamine use has been shown to cause neuronal death in the frontal cortex and hippocampus, which are areas critical for attention, working memory, and decision-making.[30] Cocaine use also leads to substantial alterations in dopamine transmission, which impairs memory consolidation and retrieval. Research by Ersche et al.[45] revealed that long-term cocaine use resulted in significant reductions in working memory capacity, with users exhibiting difficulties in holding and manipulating information for short periods. These impairments are thought to be the result of disrupted neural circuits in the prefrontal cortex and other brain regions involved in memory processing.

The presence of psychiatric disorders in individuals with substance use disorders exacerbates memory dysfunction, leading to a cycle of cognitive decline. Many individuals with SUDs experience psychiatric comorbidities, including depression, anxiety, and PTSD, which further compromise their cognitive performance. This comorbidity is particularly concerning because psychiatric disorders often lead to changes in brain structure and function that overlap with the effects of substance use, amplifying the severity of cognitive impairments. For example, depression and alcohol use disorder often co-occur, with each condition exacerbating the other's symptoms. Depression is associated with reduced hippocampal volume and altered neurotransmitter systems, while alcohol use disorders lead to shrinkage of the hippocampus and disruptions in cognitive function. This combined effect of depression and alcohol use leads to more severe memory deficits than in individuals with alcohol use disorder alone.[52] The cognitive impairments in these individuals are not limited to episodic memory but extend to other domains, including attention and executive function, which are crucial for day-to-day functioning. Anxiety disorders when combined with substance use have similar detrimental effects on memory. Chronic stress and elevated cortisol levels seen in anxiety disorders can exacerbate the neurotoxic effects of substances such as alcohol or cocaine, leading to increased damage to the brain regions responsible for memory. Furthermore, the emotional dysregulation seen in individuals with both anxiety and substance use disorders can impair cognitive flexibility and memory retrieval, making it more difficult for individuals to process and retain information.[55] PTSD is another psychiatric condition that significantly affects memory, particularly intrusive memories and impaired memory consolidation. PTSD often co-occurs with substance use disorders, especially alcohol and cannabis use, because individuals may use substances as a form of self-medication. However, substance use only exacerbates the cognitive dysfunction observed in PTSD. Chronic alcohol consumption in individuals with PTSD can worsen memory problems, particularly those related to emotion regulation and memory retrieval. The dual burden of PTSD and substance use results in heightened vulnerability to severe memory impairments, which can affect both short-term and long-term memory processes.[56]

CONCLUSION

This study examines the multidimensional effects of substance use on memory within the framework of theoretical and empirical evidence. Substance use has been identified as a complex public health issue that adversely affects cognitive function. Specifically, its effects on memory processes have been explored through various mechanisms including synaptic plasticity, information processing speed, memory trace formation, and the emergence of false memories. While existing theoretical frameworks contribute to the understanding of the negative impact of substance use on

memory, no single theory is sufficient to fully explain the complexity of this phenomenon. Therefore, it is necessary to develop holistic models that account for the interplay between biological, psychological, and environmental factors in substance use-related memory impairments.

This study had several limitations. First, the effects of substance use on memory may vary among individuals and are influenced by factors such as genetic predisposition, environmental conditions, and type of substance used. Moreover, the scarcity of longitudinal studies in the literature makes it difficult to comprehensively understand the long-term effects of substance use. The impact of substance use initiated during adolescence on cognitive development requires further investigation. Additionally, the roles of neuroplasticity and epigenetic changes in substance use-related memory impairment remain incompletely understood.

Future research should focus on several key topics. First, further experimental studies are needed to compare the specific effects of different types of substances on memory. Second, longitudinal research should be conducted to examine the progression and potential reversibility of the cognitive impairments associated with substance use. Third, genetic and neuroimaging studies should be emphasized to enhance our understanding of how individual genetic predispositions influence substance use-related memory disorders. Finally, more research is needed on the effectiveness of intervention and rehabilitation programs and how these programs contribute to the improvement of memory functions in individuals with substance use disorders.

The findings of this study have significant implications for the development of prevention and intervention strategies for substance use. It is essential to consider not only the physical aspects of substance dependence but also the cognitive and psychosocial consequences of treatment approaches. Cognitive rehabilitation techniques and psychosocial support programs designed to enhance memory function can play a crucial role in improving cognitive performance in individuals with substance disorders. In conclusion, a comprehensive and interdisciplinary approach should be adopted to mitigate the adverse effects of substance use on memory, and strategies should be developed to preserve the cognitive function of affected individuals.

ETHICAL DECLARATIONS

Referee Evaluation Process
Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
The authors declared that this study has received no financial support.

Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. UNODC. World Drug Report 2021. Vienna: United Nations Office on Drugs and Crime; 2021. Accessed [2024]. https://www.unodc.org/wdr2021
2. Green Crescent. Turkey Drug Report. Istanbul: Green Crescent Society; 2021. Accessed [2024]. https://www.yesilay.org.tr
3. Kreek MJ, Nielsen DA, Butelman ER, LaForge KS. Genetic influences on impulsivity, risk taking, stress responsiveness and vulnerability to drug abuse and addiction. *Nat Neurosci*. 2005;8(11):1450-1457. doi:10.1038/nn1583
4. Wright AC, Moody E, Browne J, Cather C. Self-defining memories among persons with mental health, substance use, cognitive, and physical health conditions: a systematic review. *Memory*. 2022;30(7):823-844. doi:10.1080/09658211.2022.2042565
5. Koob GF, Le Moal M. Drug abuse: hedonic homeostatic dysregulation. *Science*. 1997;278(5335):52-58. doi:10.1126/science.278.5335.52
6. Volkow ND, Blanco C. Substance use disorders: a comprehensive update of classification, epidemiology, neurobiology, clinical aspects, treatment and prevention. *World Psychiatry*. 2023;22(2):203-229. doi:10.1002/wps.21073
7. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. *Psychol Rev*. 1977;84(2):191-215. doi:10.1037//0033-295x.84.2.191
8. Agnew R. Foundation for a general strain theory of crime and delinquency. *Criminology*. 1992;30(1):47-88. doi:10.1111/j.1745-9125.1992.tb01093.x
9. Cohen AK. Delinquent Boys: The Culture of the Gang. Glencoe, IL: Free Press; 1955.
10. Khantzian EJ. The injured self, addiction, and our call to medicine: understanding and managing addicted physicians. *JAMA*. 1985;254(2):249-252. doi:10.1001/jama.1985.03360020081029
11. Elwyn L, Smith C. Child maltreatment and adult substance abuse: the role of memory. *J Soc Work Pract Addict*. 2013;13(3):269-294. doi:10.1080/1533256X.2013.814483
12. Goldman MS. Risk for substance abuse: memory as a common etiological pathway. *Psychol Sci*. 1999;10(3):196-198. doi:10.1111/1467-9280.00133
13. Selkoe DJ. Alzheimer's disease is a synaptic failure. *Science*. 2002;298(5594):789-791. doi:10.1126/science.1074069
14. Pitel AL, Beaunieux H, Desgranges B. Episodic memory and related processes in chronic alcoholism. *Alcohol Clin Exp Res*. 2007;31(9):1508-1519. doi:10.1111/j.1530-0277.2007.00418.x
15. Hardy J, Selkoe DJ. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *Science*. 2002;297(5580):353-356. doi:10.1126/science.1072994
16. Salthouse TA. The processing-speed theory of adult age differences in cognition. *Psychol Rev*. 1996;103(3):403-428. doi:10.1037/0033-295X.103.3.403
17. Fernández-Serrano MJ, Pérez-García M, Verdejo-García A. What are the specific vs. generalized effects of drugs of abuse on neuropsychological performance? *Neurosci Biobehav Rev*. 2010;34(3):337-346. doi:10.1016/j.neubiorev.2010.04.008
18. Roediger HL, McDermott KB. Creating false memories: remembering words not presented in lists. *J Exp Psychol Learn Mem Cogn*. 1995;21(4):803-814. doi:10.1037/0278-7393.21.4.803
19. Ranganathan M, Radhakrishnan R, Addy PH, et al, D'Souza DC. Tetrahydrocannabinol (THC) impairs encoding but not retrieval of verbal information. *Prog Neuropsychopharmacol Biol Psychiatry*. 2017;79(Pt B):176-183. doi:10.1016/j.pnpbp.2017.06.019
20. Schacter DL, Norman KA, Koutstaal W. The cognitive neuroscience of constructive memory. *Annu Rev Psychol*. 1998;49(1):289-318. doi:10.1146/annurev.psych.49.1.289
21. McDonald J, Mewse AJ, Saunders J. Effects of alcohol on source monitoring errors. *Memory*. 2000;8(6):379-389.
22. Ranganathan M, D'Souza DC. The acute effects of cannabinoids on memory in humans: a review. *Psychopharmacology (Berl)*. 2006;188(4):425-444. doi:10.1007/s00213-006-0508-y
23. Reyna VF, Brainerd CJ. Fuzzy-trace theory: an interim synthesis. *Learn Individual Differences*. 1995;7(1):1-75. doi:10.1016/1041-6080(95)90031-4
24. Brainerd CJ, Reyna VF. Fuzzy-trace theory and false memory. *Curr Dir Psychol Sci*. 2002;11(5):164-169. doi:10.1111/1467-8721.00192

25. Altura MB, Altura BT. Alcohol-induced memory impairments: neurochemical and behavioral aspects. *Neurobiol Aging*. 2001;22(3):417-423.
26. Harvey MA, Sellman JD, Porter RJ. The relationship between cannabis and cognitive functioning in schizophrenia: a systematic review. *Psychol Med*. 2007;37(7):1045-1056. doi:10.1080/09595230701247772
27. Nadel L, Moscovitch M. Memory consolidation, retrograde amnesia and the hippocampal complex. *Curr Opin Neurobiol*. 1997;7(2):217-227. doi:10.1016/S0959-4388(97)80010-4
28. Winocur G, Moscovitch M, Bontempi B. Memory formation and long-term retention. *Curr Opin Neurobiol*. 2010;20(2):161-166. doi:10.1016/j.neuropsychologia.2010.04.016
29. Dede AJO, Wixted JT, Hopkins RO, Squire LR. Autobiographical memory, future imagining, and the medial temporal lobe. *Proc Natl Acad Sci U S A*. 2016;113(48):13474-13479. doi:10.1073/pnas.1615864113
30. Volkow ND, Fowler JS, Wang GJ. The addicted human brain: insights from imaging studies. *J Clin Invest*. 2003;111(10):1444-1451. doi:10.1172/JCI18533
31. Baler RD, Volkow ND. Drug addiction: the neurobiology of disrupted self-control. *Trends Mol Med*. 2006;12(12):559-566. doi:10.1016/j.molmed.2006.10.005
32. Brooks SJ, Funk SG, Young SY, Schiöth HB. The role of working memory for cognitive control in anorexia nervosa versus substance use disorder. *Front Psychol*. 2017;8:1651. doi:10.3389/fpsyg.2017.01651
33. Jacobsen LK, Picciotto MR, Heath CJ, et al. Prenatal and adolescent exposure to tobacco smoke modulates the development of white matter microstructure. *J Neurosci*. 2007;27(49):13491-13498. doi:10.1523/JNEUROSCI.2402-07.2007
34. Ranganath C, Minzenberg MJ, Ragland JD. The cognitive neuroscience of memory for source: an update on source monitoring. *J Cogn Neurosci*. 2003;15(2):185-195.
35. Ornstein TJ, Iddon JL, Baldacchino AM, et al. Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. *Neuropsychopharmacology*. 2000;23(2):113-126. doi:10.1016/S0893-133X(00)00097-X
36. Thomasius R, Petersen K, Buchert R, et al. Mood, cognition, and serotonin transporter availability in current and former ecstasy (MDMA) users. *Psychopharmacology (Berl)*. 2006;181(4):717-726. doi:10.1177/0269881106059486
37. Pfefferbaum A, Sullivan EV. Microstructural but not macrostructural disruption of white matter in women with chronic alcoholism. *Neuroimage*. 2002;15(3):708-718. doi:10.1006/nimg.2001.1018
38. Goldstein RZ, Volkow ND. Dysfunction of the prefrontal cortex in addiction: neuroimaging findings and clinical implications. *Nat Rev Neurosci*. 2011;12(11):652-669. doi:10.1038/nrn3119
39. Payne JD, Ellenbogen JM, Walker MP, Stickgold R. The role of sleep in memory consolidation. *Learn Mem*. 2008;15(7):455-460.
40. Walker MP, Stickgold R. Sleep, memory, and plasticity. *Annu Rev Psychol*. 2006;57:139-166. doi:10.1146/annurev.psych.56.091103.070307
41. Lundqvist T. Cognitive consequences of cannabis use: comparison with abuse of stimulants and heroin about attention, memory, and executive functions. *Pharmacol Biochem Behav*. 2005;81(2):319-330. doi:10.1016/j.pbb.2005.02.017
42. Falleti E, Bitetto D, Fabris C, et al. Vitamin D receptor gene polymorphisms and hepatocellular carcinoma in alcoholic cirrhosis. *World J Gastroenterol*. 2010;16(24):3016-3024. doi:10.3748/wjg.v16.i24.3016
43. Bolla KI, Eldreth DA, Matochik JA, Cadet JL. Neural substrates of faulty decision-making in abstinent marijuana users. *Neuroimage*. 2005;19(3):1085-1094. doi:10.1016/j.neuroimage.2005.02.012
44. Morgan CA, Southwick SM, Steffian G, Hazlett G, Loftus EF. Misinformation can influence memory for recently experienced, highly stressful events. *Int J Law Psychiatry*. 2013;27(3):265-279. doi:10.1016/j.ijlp.2012.11.002
45. Ersche KD, Clark L, London M, Robbins TW, Sahakian BJ. Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology*. 2006;31(5):1036-1047. doi:10.1038/sj.npp.1300889
46. Squeglia LM, Jacobus J, Tapert SF. The influence of substance use on adolescent brain development. *Clin EEG Neurosci*. 2009;40(1):31-38. doi:10.1177/155005940904000110
47. Gooden JR, Cox CA, Petersen V, et al. Predictors of cognitive functioning in presentations to a community-based specialist addiction neuropsychology service. *Brain Impair*. 2023;24(1):54-68. doi:10.1017/BrImp.2021.38
48. Devlin P, Cao X, Stanfill AG. Genotype-expression interactions for BDNF across human brain regions. *BMC Genomics*. 2021;22(1):207. doi:10.1186/s12864-021-07525-1
49. Miller JS, Bada H, Dunworth C, Charnigo R. Recent and lifetime maternal substance use: rurality and economic distress. *Res Nurs Health*. 2023;46(5):502-514. doi:10.1002/nur.22330
50. Karlsgodt KH, Bachman P, Winkler AM, et al. Genetic influence on the working memory circuitry: behavior, structure, function and extensions to illness. *Behav Brain Res*. 2011;225(2):610-622. doi:10.1016/j.bbr.2011.08.016
51. Sepulveda-Falla D, Vélez JI, Acosta-Baena N, et al. Genetic modifiers of cognitive decline in PSEN1 E280A Alzheimer's disease. *Alzheimers Dement*. 2024;20(4):2873-2885. doi:10.1002/alz.13754
52. Umminger LF, Rojczyk P, Seitz-Holland J, et al. White matter microstructure is associated with serum neuroactive steroids and psychological functioning. *J Neurotrauma*. 2023;40(7-8):649-664. doi:10.1089/neu.2022.0111
53. McDermott TJ, Berg H, Touthang J, et al. Striatal reactivity during emotion and reward relates to approach–avoidance conflict behaviour and is altered in adults with anxiety or depression. *J Psychiatry Neurosci*. 2022;47(5):E311-E322. doi:10.1503/jpn.220083
54. Zhang Y, Feng Y, Liu L, Jiang G, Wang M. Abnormal prefrontal cortical activation during the GO/NOGO and verbal fluency tasks in adult patients with comorbid generalized anxiety disorder and attention-deficit/hyperactivity disorder: an fNIRS study. *J Psychiatr Res*. 2024;172:281-290. doi:10.1016/j.jpsychires.2024.02.053
55. Sheed A, Maharaj N, Simmons M, Papalia N, McEwan T. The role of situational factors in child-to-parent abuse: implications for assessment, management, and intervention. *Int J Offender Ther Comp Criminol*. 2023;0306624X231159895. doi:10.1177/0306624X231159895
56. Brewin CR, Miller JK, Soffia M, Peart A, Burchell B. Posttraumatic stress disorder and complex posttraumatic stress disorder in UK police officers. *Psychol Med*. 2022;52(7):1287-1295. doi:10.1017/S0033291720003025
57. Heinz AJ, Makin-Byrd K, Blonigen DM, Reilly P, Timko C, Cronkite R. Relations between cognitive functioning and alcohol use, craving, and post-traumatic stress: an examination among trauma-exposed military veterans with alcohol use disorder. *Mil Med*. 2016;181(7):709-715. doi:10.7205/MILMED-D-15-00228